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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,972	07/23/2003	Phillip I. Tarr	ALTI121522	1602

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/625,972	TARR ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2003* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *71904*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence report (2 pages)*.

DETAILED ACTION

Preliminary Amendment

1) Acknowledgment is made of Applicants' preliminary amendment filed 07/23/04.

Election

2) Acknowledgment is made of Applicants' election of cholera toxin B subunit conjugates species filed 08/13/04, in response to the species election requirement mailed 05/13/04. Because Applicants did not distinctly and specifically point out the supposed errors in the species election requirement, the election has been treated as an election without traverse (M.P.E.P § 818.03(a)).

Status of Claims

3) Claims 1-6 have been canceled via the amendment filed 07/23/04.

New claims 7-19 have been added via the amendment filed 07/23/04.

Claims 7-18 are pending and are under examination. A First Action on the Merits on these claims is issued.

Information Disclosure Statement

4) Acknowledgment is made of Applicants' information disclosure statement filed 07/19/04. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Sequence Listing

5) Acknowledgment is made of Applicants' CRF/sequence listing, which has been entered in the case on 04/05/04.

Priority

6) The instant application is a continuation of application SN 09/531,050, filed 03/20/00, *now abandoned*, which is a continuation of application SN 09/098,082, filed 06/16/1998, now US patent 6,040,421, which is a divisional application of SN 08/765,081, filed 03/26/1997, now US patent 5,798,260, which is a national stage application of SN PCT/US95/06994, filed 06/07/1995, which is a continuation-in-part the application SN 08/265,714, filed 06/24/1994, now abandoned.

Specification - Informalities

7) The instant specification is objected to for the following reason(s):

(a) The amendment introduced to the first paragraph of the specification via the

amendment of 07/23/03 does not accurately reflect the current status of an earlier application, as indicated above in italicized letters under 'Priority'. Amendment to the specification is requested.

(b) The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 C.F.R 1.75(d)(1) and M.P.E.P § 608.01(o). Correction of the following is required. In the instant case, the recitation: 'a vaccine formulation .... comprising a peptide encoded by a nucleic acid molecule that hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO: 4' lacks antecedent basis in the specification. The recitation is not found in the specification, but found in an originally presented and later canceled claim. See claim 6, as originally filed.

(c) The use of the trademarks in the instant specification has been noted in this application. For example, see first full paragraph on page 15: 'Arlacel A' and 'Arlacel C'. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar corrections to the trademarks, wherever they appear. See M.P.E.P 608.01(V) and Appendix I.

Double Patenting Rejection(s)

8) The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal

disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R 3.73(b).

Claims 7 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1 and 2 of the patent, US 6,040,421. Although the conflicting claims are not identical, they are not patentably distinct from each other, because the amino acid sequence and the vaccine claimed respectively in claims 1 and 2 of the '421 patent are encompassed within the scope of the instant claims. It would have been obvious to one of ordinary skill in the art at the time the invention was made to add an art-known pharmaceutical carrier to the product of the claims of the '421 patent, since it is conventional and routine in the art of vaccines to add such a carrier to a bacterial product meant for use as a vaccine or immunogen for the ease of administration.

Rejection(s) under 35 U.S.C § 101

9) 35 U.S.C. § 101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this cycle.

10) Claim 7 and those dependent therefrom are rejected under 35 U.S.C § 101 as being directed to a non-statutory subject matter.

The independent claim 7 does not sufficiently distinguish over a formulation comprising a peptide or an immunogenic fragment thereof as it exists naturally, for example, on the surface of a microbe, or sloughed off the microbial surface and being present in nature, for example, in naturally occurring clean water, because the claim does not particularly point out any non-naturally occurring differences between the claimed product and the naturally occurring product. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980)*. The claims should be amended to indicate the hand of the inventor, e.g., by replacing the recitation 'a peptide' with the limitation '-- an isolated peptide-- if descriptive support exists for such a limitation in the instant application. See MPEP 2105.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

11) Claims 7-19 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 7 includes the limitation: 'the nucleotide sequence *complementary to* SEQ ID NO: 4' [Emphasis added]. Claim 16 includes the limitation: 'a peptide encoded by a nucleic acid molecule that hybridizes under stringent conditions to ..... *its complement*' [Emphasis added]. However, there appears to be no descriptive support in the instant specification for a peptide encoded by a 'complement' of any nucleotide sequence. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific part(s), lines and pages of the disclosure, as originally filed, for the limitations identified above, or to remove the new matter from the claims.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (Scope of Enablement)

12) Claims 7-19 are rejected under 35 U.S.C § 112, first paragraph, because the specification while being enabling for a whole cell vaccine formulation comprising an adhesin-producing strain of *Escherichia coli* O157:H7, wherein the whole cell vaccine reduced the fecal shedding rates of *Escherichia coli* in calves, does not reasonably provide enablement for a vaccine formulation for preventing and/or treating a generic infection by any pathogenic member of the family *Enterobacteriaceae* in any mammalian subject, or to promote the clearance of 'the pathogenic enterobacteriaceae from the gastrointestinal tract' of a mammalian subject, comprising a peptide encoded by a nucleic acid molecule that hybridizes to the nucleotide sequence of SEQ ID NO: 4, or its full or partial complement under stringent conditions as claimed in a broad sense.

The instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;

- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant case, the claims encompass a vaccine formulation comprising a peptide encoded by a nucleic acid molecule that hybridizes to the nucleotide sequence of SEQ ID NO: 4, or its full or partial complement under stringent conditions. The stringent conditions are not specified or not recited. The specification does not precisely describe the precise conditions that qualify as 'stringent' conditions. The precise structure of a nucleic acid molecule, which hybridizes under the generically recited stringent conditions to the nucleotide sequence of SEQ ID NO: 4, is not described. The vaccine formulation is meant for 'preventing and/or treating infection' by a pathogenic *Enterobacteriaceae* in a mammalian subject and 'to promote the clearance' of the pathogenic *Enterobacteriaceae* from the gastrointestinal tract of an infected mammalian subject. However, no evidence is of record that establishes that a peptide encoded by a nucleic acid molecule that hybridizes to the nucleotide sequence of SEQ ID NO: 4, or its full or partial complement under the generically recited stringent conditions, does in fact has the ability to prevent and/or treat a generic infection by any pathogenic member of the family *Enterobacteriaceae* in a human or non-human mammalian subject, and to promote the clearance of a 'pathogenic *Enterobacteriaceae* from the gastrointestinal tract of a generically infected subject. Since the stringent conditions are not described, even nine to twelve contiguous nucleotide bases identical to the nucleotide bases of SEQ ID NO: 4 would hybridize with the nucleotide sequence of SEQ ID NO: 4, especially under low stringent conditions. The recited 'peptide' in the claimed vaccine formulation encompasses a peptide of any length and from any part of the protein encoded by the nucleotide sequence of SEQ ID NO: 4. It should be noted that 4, 5 or 6 contiguous amino acid residues encoded by such a nucleotide sequence would qualify as a peptide as recited. However, there is no showing within the instant specification that such a peptide would be effective in serving as a 'vaccine formulation' capable of 'preventing and/or treating infection' by a myriad of possible pathogenic members of the family *Enterobacteriaceae* in a human or non-human mammalian subject, or promoting the clearance of the pathogenic *Enterobacteriaceae* from the gastrointestinal tract of a generically infected subject. As recited, the term 'mammalian subject' encompasses a

human and a non-human subject having infection by any pathogenic member of the family *Enterobacteriaceae*. *Enertobacteriaceae* is a large bacterial family which includes a myriad of diverse pathogenic bacteria, including several species of *Salmonella*, *Shigella*, *Escherichia*, *Proteus* etc. The ability to prevent and treat an infection, or promote the clearance from the gastrointestinal tract of a mammalian subject of any species of any of these pathogenic bacterial members of the family *Enertobacteriaceae* requires a showing that the 'peptide' in the claimed vaccine is shared by all species of all these pathogenic bacterial members of the family *Enertobacteriaceae*. However, such a showing is lacking in the instant specification. A bacterial member of the family *Enertobacteriaceae* that is pathogenic to a human subject need not be pathogenic in a non-human subject. For example, *E. coli* O157:H7 known to be pathogenic in some human subjects is a commensal in the gastrointestinal tract of some non-human mammalian subjects such as for example, cattle. Concrete evidence is critical because the term 'vaccine' requires that the claimed peptide element in the vaccine is protective against specific pathogens or diseases. The prophylactic and therapeutic efficacy of a microbial peptide is not always predictable. It is well known in the art that, of a myriad of polypeptides or peptides may be produced by a bacterial or microbial pathogen, but not all polypeptides elicit a pathogen-specific immune response that is protective against the pathogen. The art of vaccines recognizes the unpredictability associated with whether or not an antigen or immunogenic component derived from a microbial pathogen is immunoprotective. For instance, Ellis RW (*Vaccines*, (Eds) Plotkin *et al.*, W.B. Saunders Company, Philadelphia, Chapter 29, 568-575, 1988, see page 571, second full paragraph) reflected this problem in the teaching that the key to the problem of vaccine development "is the identification of that protein component of a ..... microbial pathogen that itself can elicit the production of protective antibodies ..... and thus protect the host against attack by the pathogen". It is emphasized that predictability or unpredictability is one of the *Wands* factors for enablement. In the instant case, the specification fails to teach or show that the peptide of any size obtained from any part of a protein encoded by a nucleic acid molecule that hybridizes to the nucleotide sequence of SEQ ID NO: 4, or its full or partial complement under stringent conditions, alone or in combination with other antigens, does in fact induce a prophylactic and therapeutic immune response that is protective against any member of the family *Enterobacteriaceae*.

The claims must be enabled over their whole breadth. The *Webster's II New Riverside University Dictionary* (1984) defines the term 'prevent' as 'to keep from happening'. The term 'infect' is defined in the *Illustrated Stedman's Medical Dictionary* (24th Edition, 1982) as 'to enter, invade, inhabit, or to dwell internally'. Infection by a pathogenic *Enterobacteriaceae* encompasses enterobacterial cell invasion and growth or multiplication of the bacteria therein. There is absolutely no showing within the instant specification that the peptide in the claimed vaccine formulation has the ability to keep the enetrobacterial cell entry, cell invasion and internal cellular dwelling from happening, and thereby preventing the infection. This is critical because there is no predictability that a microbial peptide would be prophylactic or therapeutic against any infection caused by any member of the family *Enterobacteriaceae*, or even the homologous member of the family *Enterobacteriaceae*. See above for the teachings of Ellis RW. It is noted that Figure 1 only supports the role of an adhesin-producing strain of *Escherichia coli* as a whole cell vaccine by reducing the fecal shedding rates of *Escherichia coli* O157:H7 in calves.

Furthermore, the peptide claimed in the vaccine formulation of claim 17 or 18 is derived from a recombinant organism or a transgenic plant. However, there is no evidence in the instant specification showing that the peptide derived from a recombinant organism or a transgenic plant has the ability to prevent and/or treat an infection by a pathogenic *Enterobacteriaceae* in a mammalian subject. At lines 2-6 of page 18, the specification states that animals are put on such feed in the several days or weeks prior to shipment of slaughter, **provided** control challenge experiments show that the recombinant adhesin, expressed in plants which are then fed to the animals, promotes clearance of ***E. coli O157:H7*** from the gastrointestinal tract of such **animals**, thereby reducing the load of **this pathogen** that enters the production line in abattoirs. However, this is a mere speculation about a recombinant adhesin expressed in plants, which is planned to be fed to 'animals' to promote clearance of one specific bacterium of the family *Enterobacteriaceae* [which cannot really be called as a pathogen in every animal or mammal] from the gastrointestinal tract of such animals. Concrete *in vivo* data or correlative *in vitro* data are lacking.

Undue experimentation would have been required to practice the invention as claimed currently due to the lack of specific teaching and guidance as to how to identify and obtain the recited nucleotide sequences and peptides of the claims, the unpredictability associated with the

preventive or therapeutic ability of such a peptide against any pathogenic member of the entire family *Enterobacteriaceae*, the quantity of experimentation necessary, the lack of evidence and of working examples in the specification enabling the full scope of the claimed invention, the unpredictability involved in the production of a peptide functional as a prophylactic or therapeutic vaccine, and the breadth of the claims. The reproducible practicing of the invention as claimed would have been be well outside the realm of routine experimentation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims. The enablement (scope) provisions of 35 U.S.C. § 112, first paragraph, are not met.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

13) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

14) Claims 7-19 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 7 is vague and indefinite in the recitation: 'its complement', because it is unclear what is encompassed in this 'complement'. How much of the original structure of SEQ ID NO: 4 should be retained in a nucleotide sequence such that it qualifies as a 'complement' is not clear.

(b) Claim 7 is vague and indefinite in the recitation: 'complementary to SEQ ID NO: 4', because it is unclear what is encompassed in this limitation. How much of the original structure of SEQ ID NO: 4 should be retained in a nucleotide sequence such that it qualifies as a sequence 'complementary to SEQ ID NO: 4' is not clear.

(c) Claims 7 and 16 are vague and indefinite in the recitation 'under stringent conditions'. It is unclear what conditions qualify as 'stringent' conditions. Are these low, medium or high stringent conditions?

(d) Claim 15 contains the trademark/trade name 'Arlacel'. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte*

Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe 'Arlacel A, Arlacel C' and, accordingly, the identification/description is indefinite.

(e) Claim 17 is vague and indefinite in the limitation: 'derived', because it is unclear what is encompassed in the limitation 'derived'. Does 'derived' mean isolated, purified, separated, extracted, or expressed? What is involved or included in the process of deriving is not clear.

(f) Claim 19 is vague, indefinite and confusing in the limitation: 'clearance of the pathogenic enterobacteriaceae', because the term *Enterobacteriaceae* represents a bacterial family. It is unclear how the clearance can be of the family *Enterobacteriaceae* as opposed to a pathogenic bacterial member of the family *Enterobacteriaceae*.

(g) Claim 16 is confusing and/or does not appear to have proper antecedence in the limitation: 'formulation of Claim 7 which comprises a peptide'. Claim 16 depends from claim 7, which already recites 'a peptide'. Is 'a peptide' recited in the dependent claim 16 different from the one recited in claim 7? If not, it is suggested that Applicants provide proper antecedence by replacing the recitation 'which comprises a peptide that' in line 1 of claim 16 with --wherein said peptide--.

(h) Claims 8-19, which depend directly or indirectly from claim 7, are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, because of the vagueness or indefiniteness in the base claim(s) identified above.

Rejection(s) under 35 U.S.C. § 102

15) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
> **(e)(2)** a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

16) Claims 7-11 and 14-19 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Brenton (US 6,605,709).

Instant claims are not afforded priority to the international application, since the recitation 'the nucleotide sequence complementary to SEQ ID NO: 4' is not supported in the prior international application. It is noted that the recitation 'sequence complementary to SEQ ID NO: 4' in claim 7 encompasses sequences that are partially complementary to SEQ ID NO: 4. The generic recitation 'stringent conditions' in claim 7 encompasses low stringency conditions.

Brenton disclosed a vaccine for therapeutic and prophylactic use in an individual against *Proteus mirabilis* infections comprising a pharmaceutically acceptable carrier and a peptide encoded by a nucleic acid molecule that has several long stretches of 100% sequence identity with the instantly recited SEQ ID NO: 4. The peptide or the polypeptide fragment is recombinant, immunogenic, and is capable of eliciting a humoral and/or a cellular immune response in a host animal. The peptide has the ability to inhibit the binding of *Proteus mirabilis* with an interactive polypeptide. See the attached sequence search report; first, second and third full paragraphs in column 38; third and fourth full paragraphs in column 9; lines 62 and 63 in column 12; lines 27-42 of column 14; last paragraph in column 5; paragraph bridging columns 5 and 6; and columns 29 and 30; first and second full paragraphs in column 30; paragraph bridging columns 37 and 38; columns 37-40; columns 10 and 11; columns 6-12; and columns 17-22 and 27-30. The bacterial genus *Proteus* is taught to be a member of the family *Enterobacteriaceae* (see lines 22 and 23 of column 1), and *Proteus mirabilis* is taught to be a pathogenic member which causes clinical conditions such as bacteremia and various other disease conditions (see last full paragraph in column 1). The vaccine comprising the immunogenic polypeptide fragment is useful for both preventing and treating *Proteus mirabilis* infection (see last two full paragraphs in column 40). The vaccine composition comprises a stabilizer and is administered parenterally or orally, and the oral administration is preferred for inducing protection against infection by *Proteus mirabilis* (see lines 28-38 in column 39; fourth full paragraph in column 46; and paragraph bridging columns 39 and 40). The vaccine comprises liposomes or adjuvants, such as, cholera toxin B subunit conjugates or monophosphoryl lipid A (see fourth full paragraph in column 39). The vaccine is in the form of enteric-coated capsules (see first full paragraph in column 40). That the prior art nucleic acid molecule comprising several long stretches of 100% identical nucleotide sequences hybridizes to the instantly recited SEQ ID NO: 4 at least under low stringent conditions is inherent from the

teachings of Brenton.

The limitation 'produced in a transgenic plant' in claim 18 represents a process limitation in a product claim. When claims are product-by-process claims, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. The phrase 'produced in a transgenic plant' does not structurally distinguish the claimed peptide product from the prior art product. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art peptide differs from that of the instantly recited peptide.

Claims 7-11 and 14-19 are anticipated by Brenton.

Rejection(s) under 35 U.S.C. § 103

17) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

18) Claims 12 and 13 are rejected under 35 U.S.C § 103(a) as being unpatentable over Brenton

(US 5,380,655) as applied to claim 7 above, and further in view of Hansen *et al.* (US 5,380,655).

The teachings of Brenton are explained above, which do not expressly teach their peptide vaccine further comprising sorbitol or gelatin as a stabilizer. However, it was routine and conventional in the art at the time the invention was made to stabilize a vaccine composition by adding sorbitol or gelatin as a stabilizer to a peptide-containing vaccine. For instance, Hansen taught the addition of sorbitol or gelatin as a stabilizer to a peptide-containing vaccine (see paragraph bridging columns 7 and 8).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Hansen's sorbitol or gelatin stabilizer to Brenton's peptide vaccine to produce the instant invention, with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of stabilizing Brenton's peptide vaccine as it was routine and conventional in the art of vaccines to do so as taught by Hansen.

Claims 12 and 13 are *prima facie* obvious over the prior art of record.

Objection(s)

19) Claims 7 and 19 are objected to for the following reasons:

(a) Claims 7 and 19 are incorrect in the recitation: 'Enterobacteriaceae' (see line 2 of claim 7 and line 4 of claim 19). To be consistent with the practice in the art, it is suggested that Applicants replace the limitation with --*Enterobacteriaceae*--.

(b) The recitation in line 2 of claim 19 'enterobacteriaceae' is inconsistent with the recitation 'Enterobacteriaceae' in 4 of the claim. It is suggested that Applicants replace the recitation with --*Enterobacteriaceae*--.

Remarks

20) Claims 7-19 stand rejected.

21) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of amendments, responses or papers is (703) 872-9306.

22) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

23) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

November, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER

SEQ ID NO: 4

RESULT 10
US-09-543-681A-4908
; Sequence 4908, Application US/09543681A
; Patent No. 6605709
; GENERAL INFORMATION:
; APPLICANT: GARY BRETON
; TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO PROTEUS MIRABIL
; TITLE OF INVENTION: DIAGNOSTICS AND THERAPEUTICS
; FILE REFERENCE: 2709.1002-001
; CURRENT APPLICATION NUMBER: US/09/543,681A
; CURRENT FILING DATE: 2000-04-05
; PRIOR APPLICATION NUMBER: US 60/128,706
; PRIOR FILING DATE: 1999-04-09
; NUMBER OF SEQ ID NOS: 8344
; SEQ ID NO 4908
; LENGTH: 684
; TYPE: PRT
; ORGANISM: Proteus mirabilis
US-09-543-681A-4908

Alignment Scores:

Pred. No.:	3.16e-79	Length:	684
Score:	956.50	Matches:	239
Percent Similarity:	51.86%	Conservative:	138
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US-10-625-972-4 (1-2091) x US-09-543-681A-4908 (1-684)

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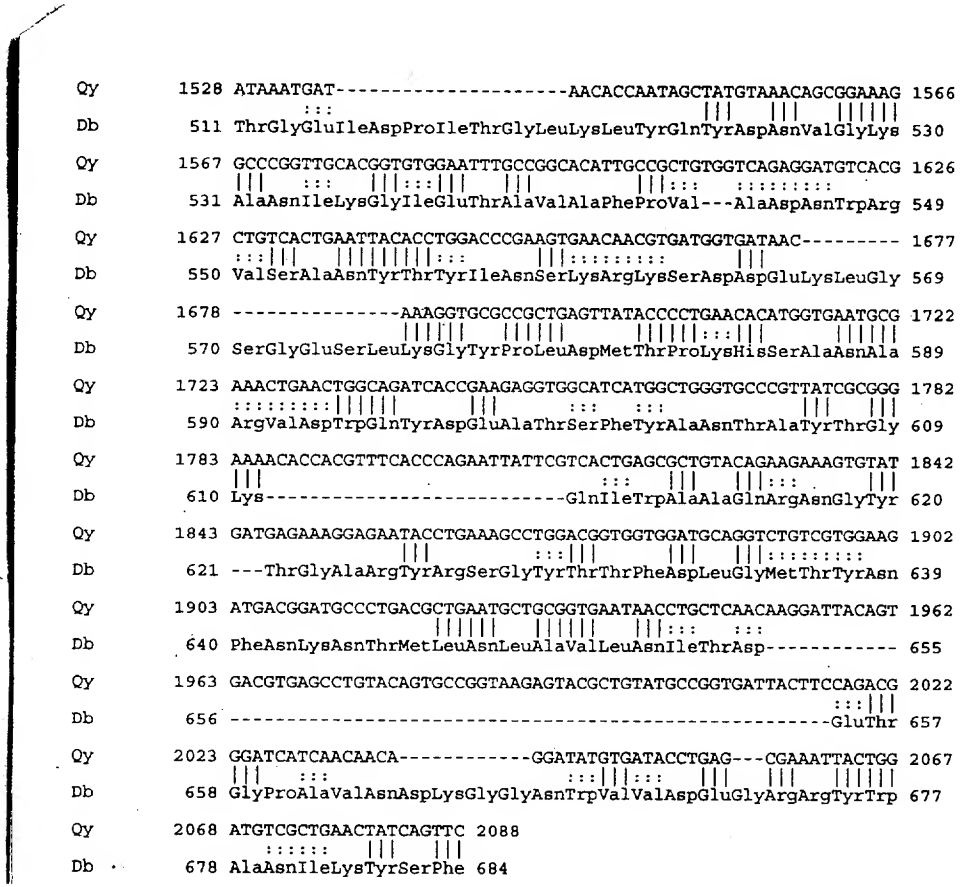
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